

Remarks

Applicant has carefully considered this Application in connection with the Examiner's Action, and respectfully requests reconsideration of this Application in view of the foregoing amendment, and the following remarks.

Claims 3 and 5 – 9 are presently pending in this Application. Claims 1 and 2 are canceled. Claims 3, 5, 6 are amended, with support for the amendments found in the claims as previously presented. No new matter has been added.

Applicant thanks the Examiner for the withdrawal of the prior rejection under 35 U.S.C. § 112, first paragraph, as well as the prior rejection of Claim 3 under 35 U.S.C. § 112, first paragraph.

I. Rejection under 35 U.S.C. § 103(a)

Claims 1 – 4, and 6, 7 and 9 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ormerod et al. (WO 99/24036) in view of Hardman et al. Applicant respectfully traverses the rejection.

The Examiner cites Ormerod for teaching topical formulations and method of treatment of a dermatological condition comprising an immunosuppressive macrolide and a permeation modulator, which when applied to the skin produces a minimal systemic effect.

Ormerod, however, is solely directed to topical formulations and teaches away from the use of systemic preparations. Ormerod discloses formulations in which significant absorption of the said drugs into the systemic system is avoided. (Ormerod, p. 5, lines 27 – 32) The formulations of Ormerod are specifically suited for passage of drug across the stratum corneum, while avoiding systemic exposure, thereby producing minimal systemic effect. (Ormerod, p. 3, lines 7 – 10 and p. 3, lines 13 – 21) Moreover, the permeation modulator is an expressly essential and required element of the composition taught by Ormerod.

Nowhere does Ormerod teach an immunosuppressive-agent-formulation for oral or i.v. administration as expressly taught by Applicant for treating dermatological conditions as required by Applicant's Claim 3.

The Examiner goes on to cite Hardman for teaching the utility of retinoids and antibiotics in the treatment of dermatological diseases. Hardman does not teach, nor does Hardman even mention, the macrolide T-cell immunomodulator 33-epichloro-33-

desoxyascomycin, nor any immunosuppressive agents for that matter, alone or in combination with a retinoid, for treating dermatological conditions. Furthermore, a retinoid in combination with an antibiotic is not the equivalent of a retinoid in combination with a macrolide T-cell immunomodulator or immunosuppressive, such as 33-epichloro-33-desoxyascomycin. Specifically, an antibacterial does not have the same mode of action on inflammation as an immunomodulator, such as 33-epichloro-33-desoxyascomycin. Hardman also fails to teach a synergistic combination of compounds in a manner expressly claimed by Applicant's Claim 3.

Applicant respectfully asserts that the references cited by the Examiner, singularly or in combination, fail to teach the limitations of Applicant's claims because the references fail to teach or suggest a method of treating a condition, comprising administering to a subject suffering from a dermatological disease, such as eczema, atopic dermatitis, acne, psoriasis, skin aging, sun damage, post-peel erythema or stretch marks, a synergistically effective amount of a composition comprising 33-epichloro-33-desoxyascomycin in combination or association with etretinate, isotretinoin or tazarotene, wherein administration is oral, intravenous or topical. As such, the references – even when combined – fail to teach each and every element of Applicant's claimed invention.

At the time of the invention, not only was there simply no disclosed use of 33-epichloro-33-desoxyascomycin in combination with a retinoid for the treatment of dermatological diseases, there was no suggestion or motivation in the art to arrive at Applicant's invention. Applicant respectfully asserts that a person of ordinary skill in the art would not be motivated or suggested to combine the references as suggested by the Examiner.

For instance, while the Examiner cites *In re Kerkhoven* as the basis for the prima facie obvious rejection, the Examiner has not considered an important aspect of that case: the holding was based on the absence of unexpected results. Applicant discusses, at paragraph 0002 of Applicant's published application, the surprising and unexpected nature of the results associated with Applicant's invention. Specifically, Applicant's Table shows results of combination treatment over individual compounds for treating atopic dermatitis. Neither compound, when administered individually, had the same effect on AD as did the administration of the combination of compounds. It was entirely unknown in the art at the

time of the invention that 33-epichloro-33-desoxyascomycin could be combined with a retinoid in a synergistic manner for more effective treatment of dermatological diseases.

Furthermore, as noted above in the discussion of Ormerod, previous use of immunosuppressive macrolides for dermatological conditions sought specifically to avoid systemic dissemination. For instance, Ormerod required a permeation modulator to target partial absorption into the dermis, thereby avoiding adverse side effects related with systemic absorption of immunosuppressives. (See Ormerod, Page 5, lines 10 – 33.) Thus, Applicant respectfully asserts that it is not *prima facie* obvious, as the Examiner contends, to merely combine two compositions taught in the prior art useful for a similar purpose. Applicant believes that the Examiner's conclusion could only be drawn through impermissible hindsight.

No use of a synergistically effective amount of 33-epichloro-33-desoxyascomycin in combination with a retinoid for treating a dermatological condition, as required by Applicant's claims is taught or suggested by the references cited by the Examiner. As such, Applicant respectfully requests that the rejection under 35 U.S.C. §103 (a) be reconsidered and withdrawn.

II. Rejection under 35 U.S.C. § 103(a)

Claim 5 is rejected under 35 U.S.C. §103(a) as being unpatentable over Ormerod et al in view of Hardman and further in view of Remington.

For the reasons stated above in regard to the rejection, and in light of the amendment to Claim 5, Applicant respectfully asserts that the rejection is moot. As such, Applicant respectfully requests that the rejection be reconsidered and withdrawn.

III. Rejection under 35 U.S.C. § 103(a)

Claims 1 – 3 and 7 – 9 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Vaishnaw et al. (US 2003/0185824). Applicant respectfully traverses the rejection.

The Examiner cites Vaishnaw for teaching compositions and methods for treating or preventing an epidermal or dermal disorder including psoriasis and atopic dermatitis.

Vaishnaw discloses an inhibitor of the CD2/LFA-3 interaction in combination with an auxiliary agent. In a preferred embodiment, the auxiliary agent is chosen from a multitude of agents, including retinoids or pimecrolimus, among many others. Vaishnaw does not

disclose the compositions of the present invention, as the Examiner suggests, let alone a synergistic effect when treating a dermatological condition. Specifically, Vaishnaw does not teach a retinoid in combination with pimecrolimus as Examiner contends, rather, Vaishnaw teaches either a retinoid or pimecrolimus in combination with a CD2-binding agent. To simply leave out the active principle of the composition as disclosed in Vaishnaw – the CD2-binding agent – would require the person of skill to disregard the invention as disclosed by Vaishnaw. Again, such a conclusion can only be made in hindsight and by ignoring large parts of the disclosure and explicit teachings of Vaishnaw.


Applicant respectfully asserts that no use of a synergistically effective amount of 33-epichloro-33-desoxyascomycin in combination with a retinoid for treating a dermatological condition, as required by Applicant's claims is taught or suggested by the reference cited by the Examiner. As such, Applicant respectfully requests that the rejection under 35 U.S.C. §103 (a) be reconsidered and withdrawn.

IV. Conclusion

In view of the foregoing, Claims 3, and 5 – 9 are in condition for allowance, and Applicant earnestly solicits a Notice of Allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this Application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration to this Amendment and Reply is respectfully requested.

Respectfully submitted,
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